A Dissertation On

CLINICAL STUDY OF THYROID RELATED ORBITOPATHY

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CERTIFICATE

This is to certify that this dissertation titled "**CLINICAL STUDY OF THYROID RELATED ORBITOPATHY**" is a bonafide work done by Dr.S. NEHRU, M.S. Post Graduate Student of Ophthalmology Regional Institute of Ophthalmology, Govt. Ophthalmic Hospital, Egmore, Chennai – 600 008 attached to Chennai Medical College, during the academic year 2004 – 2006.

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INTRODUCTION

Graves' orbitopathy has been known for close to 200 years. Since its first description Graves' disease with its complex manifestations and unpredictable clinical course has fascinated and frustrated internists, surgeons, ophthalmologists and immunologists alike. It is enigmatic by what mechanism the thyroid gland and ocular tissues interact, and in what ways the clinician may modify possible inter relationships.

The literature is replete with diverse nomenclature, diagnostic groupings, classifications and eponyms, making it difficult to appreciate the nature of this disorder as it presents in the patient.

Rootman refers to the orbital changes and ocular abnormalities as Graves' orbitopathy because it is an orbital rather than an ophthalmic process. Mc Kenzie has given the most pragmatic current definition of Graves' disease:

A multisystem disorder of unknown etiology characterized by one or more of three clinical entities

1. hyperthyroidism associated with diffuse hyperplasia of the thyroid gland
2. infiltrative ophthalmopathy
3. infiltrative dermopathy(localized pre-tibial myxoedema).

While thyroid and eye disturbances frequently co-occur, the manifestations in these two organs run a distinctly separate clinical course.

Patients with thyroid disease often end up in Ophthalmologist's Clinic, because of the problem of exophthalmous & lid retraction which cosmetically and socially lead to many problems in day to day life. So the role of ophthalmologists in thee patients is to effect a therapy that will restrict the progression of Thyroid Related Orbitopathy & to reduce the lid retraction either by medical or surgical modalities.

HISTORY

As early as the 12th century, the Persian writings of Sayyid Ismail Al – Jurjani described that exophthalmos is related to goiter. Parry in 1786 described Parry's disease compromising-goitre, tachycardia and protrusion of eyes. Flajani(1802) and Calebhillier followed by Graves'(1835) after whom the eponym of Graves' disease followed, described an enlarged thyroid associated with palpitation and protrusion of eyes.

Basedow (1799-1854) described exophthalmos as due to hypertrophy of orbital tissue caused by disordered circulation and discussed the three cardinal symptoms of exophthalmos, goitre and tachycardia. Hence the condition is frequently termed Basedow's disease in German literature. Rehn (1884) and Moebius (1887) were the first to point to hyperthyroidism as the essential cause of exophthalmos.

Malignant exophthalmos (Rosenbaum 1937; Ruedeman 1937) is a condition where the exophthalmos tends to be pronounced and intractable even in the absence of an associated thyrotoxicosis.

This multiplicity of nomenclature was due to the ignorance of the aetiology of the condition. The autoimmune aetiology, which is proven, now has simplified the nomenclature as Graves' disease. There are still many facets of this fascinating subject yet to be solved.

PIONEERS IN THE FIELD OF TRO

Robert James Graves (1796–1853).

Carl Adolph Basedow (1799-1854)

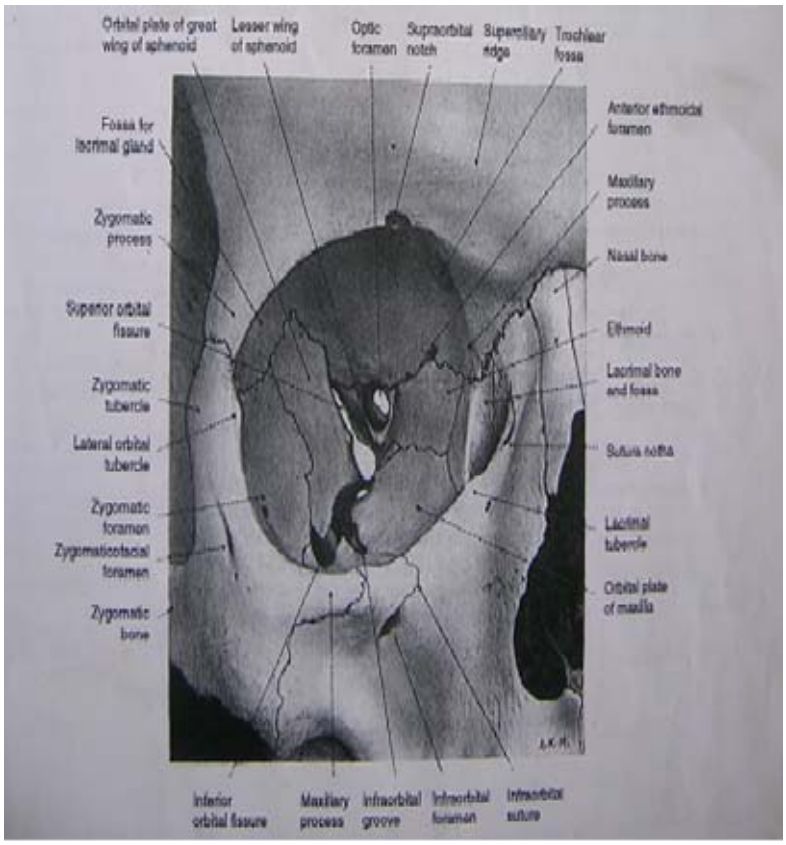
ANATOMY OF THE ORBIT

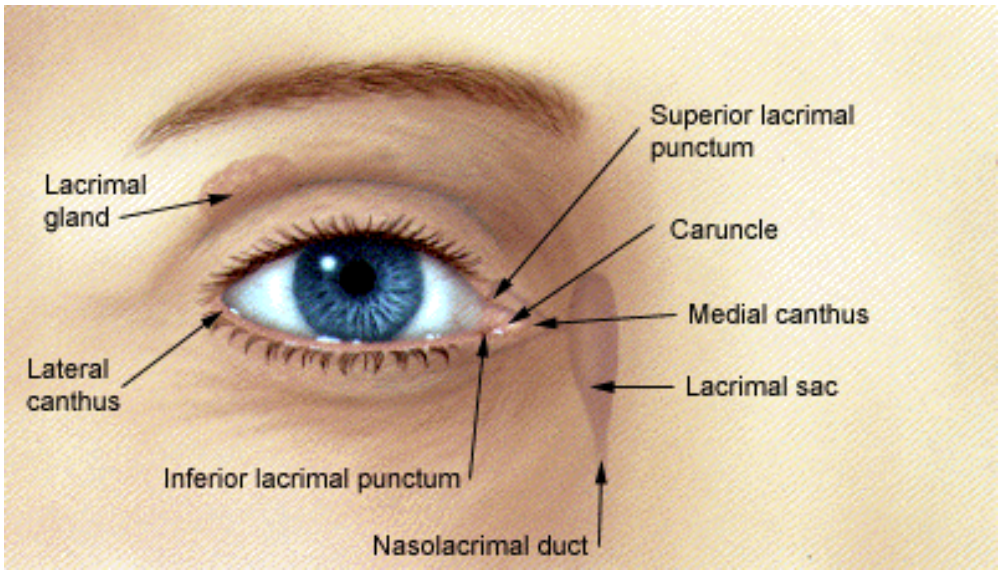
The human orbital cavities are placed on either side of the sagittal plane of the skull between cranial and facial parts encroaching about equally on both. The orbit is essentially a socket containing the eyeball and the muscles, nerves, and vessels supplying it. Rest of the space in the orbit is occupied by fat, connective tissue and lacrimal gland. It also transmits certain vessels and nerves to supply areas around the orbital aperture.

The orbit is composed of seven bones: frontal, sphenoid, zygomatic, maxillary, palatine, lacrimal and ethmoid. In shape, it is roughly a quadrilateral pyramid with an apex, base and four walls, which is directed forwards, laterally, and slightly downwards.

The apex corresponds to the optic foramen, the base corresponds to the orbital margin, which opens on the face and the four walls, which form the roof, floor, lateral wall and the medial wall. The floor and the roof are roughly triangular, the lateral and medial walls quadrilateral and the floor does not reach up to the apex. The medial walls of the two orbits are parallel to each other. The orbital opening on the face does not correspond to the coronal plane and is inclined to it at an angle of 15^0 so that the medial wall reaches a more anterior position than the lateral wall. The medial wall is the thinnest, the floor the shortest and the lateral wall the strongest.

RIGHT ORBIT - VIEWED ALONG ITS AXIS
(Courtesy Wolff's Anatomy of the Eye & Orbit)





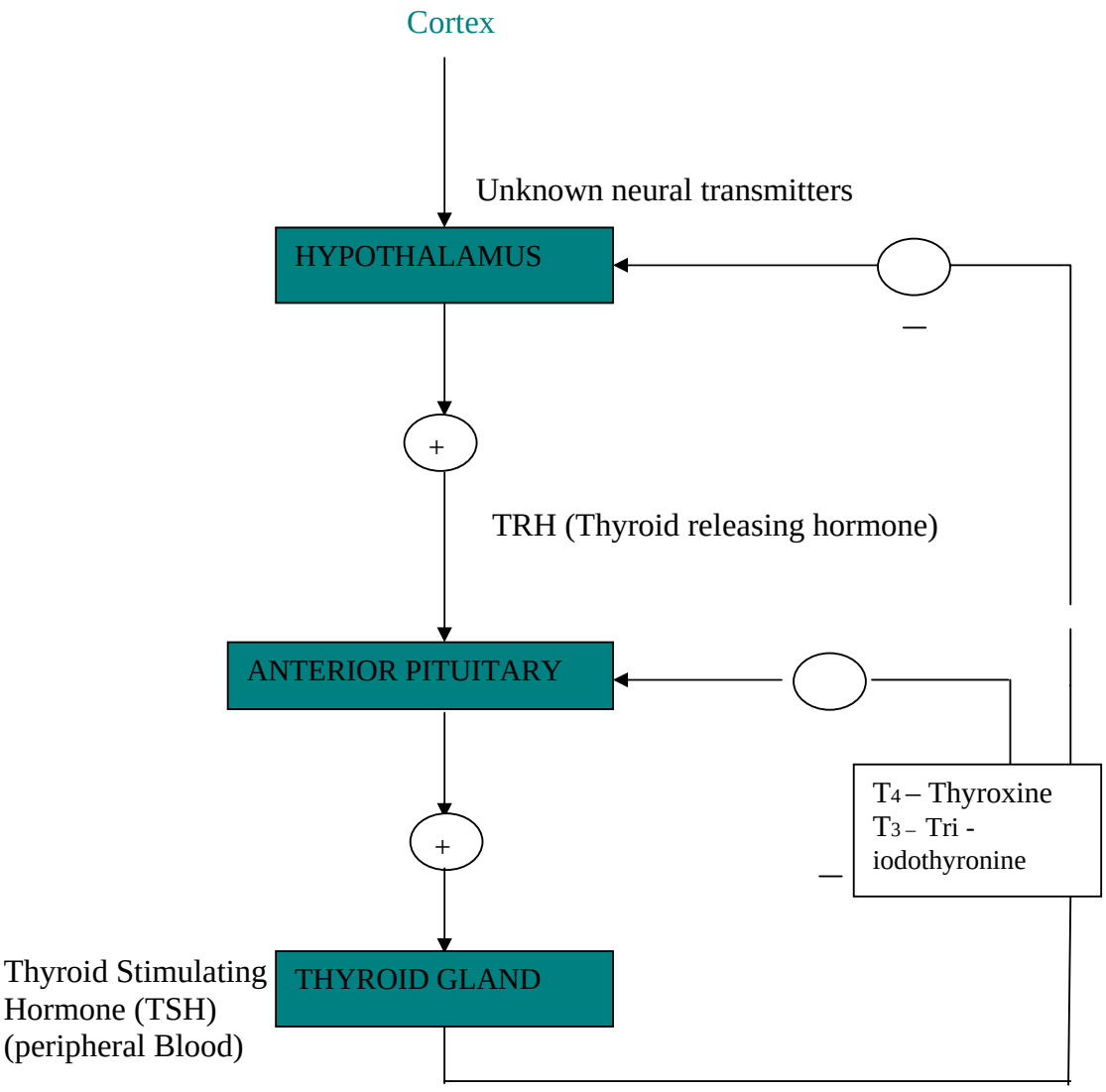
EMBRYOLOGY AND DEVELOPMENT OF THE ORBIT

The orbit develops from the mesoderm surrounding the optic vesicle and the optic stalk. The orbital mesoderm is derived from several sources. Above the mesodermal capsule of the forebrain, forms the roof of the orbit. Below and laterally, the maxillary process forms the floor and lateral walls of the orbit. Medially, the frontonasal process forms the medial wall of the orbit. The pre and orbitosphenoid, contributes to the roof, medial and lateral walls posteriorly.

Of the seven orbital bones, the first to be laid down is the ethmoid at 6-8 weeks of gestation. The trochlea begins to consolidate at about 9 week of gestation. Except for the lesser wing of the sphenoid, which is initially cartilaginous, all other bones of the orbit are membranous and begin to ossify during the third month. Fusion takes place between the sixth and seventh month. At birth orbit is 55% of adult size. It reaches 79% at 3 years and 94% at 7 years of age. Generally, orbits do not grow much after 7 years. The growth of cranium, face and paranasal sinuses influence the shape and size of the orbit. The angle subtended by the orbital axes is nearly 180^0 at first and diminishes to approximately 105^0 at 3 months of gestation and at birth; the angle is 71^0. By 3 years of age the orbital axes attains its adult condition of 68^0.

THE PHYSIOLOGY OF THYROID GLAND AND ITS DISEASE STATES

The pituitary – Thyroid Axis



Hypothalamic TRH stimulates (+) pituitary, which releases thyroid-stimulating hormone, which stimulates (+) the thyroid. Levels of T4 and T3 in blood provide information about FEED BACK REGULATION OF Thyroid function gland by the pituitary.

DISEASE STATES OF THE THYROID GLAND

The Thyroid gland is commonly affected by the following conditions:

A:Thyroiditis

B: Hyperthyroidism

C: Hypothyroidism

Hyperthyroidism – Also known as thyrotoxicosis, is a state in which there is an excess of circulating thyroid horomones, namely T3 or T4. It may be primary or secondary. Primary thyrotoxicosis is also known as Graves' disease. The gland is diffusely enlarged and there are signs of a hypermetabolic state. The eyes may or may not be involved. Secondary thyrotoxicosis occurs when a patient with a previously abnormal gland (eg.Nodular goiter) assumes a hyper functional state.

Hypothyroidism - implies the clinical manifestations due to lack of thyroid hormone. It may be idiopathic atrophic, Post – ablative (post surgical / external radio therapy), auto – immune, drug induced, congenital, secondary to pituitary or hypothalamic disease.

Cretinism occurs in children and infants due to dysgenesis of thyroid gland or metabolic errors or chronic iodine deficiency in endemic regions.

CLINICAL FEATURES OF HYPERTHYROIDISM

	Symptoms	Signs
General	Anxiety,tremulousness,generalized weakness, heat intolerance, skin thinning and tanning, brittle hair, pruritis.	Restlessness, objective weight loss, excessive sweating, hair thinning.
CVS	Palpitations, irregular beats and shortness of breath.	Tachycardia, increased pulse pressure, ectopic beats, atrial fibrillation, sick sinus syndrome, cardiac failure.
CNS	Hyperactivity, muscle weakness, apathy in older age.	Fine tremors, hyper-reflexia, proximal muscle weakness, and periodic paralysis.
GIT	Diarrhoea(non-infective)	Rapid bowel transit time, steatorrhoea.
Reproductive system	Oligomenorrhoea or amenorrhoea, impotence.	Gynecomastia, infertility.
Thyroid gland	Enlargement of gland, neck pressure symptoms	Diffuse or nodular goiter, bruit, thrill.
Eye	Stare, gritty sensation, increased lacrimal secretion, diplopia, decreased colour and contrast vision, dry eyes, increased sensitivity to light, angry looking eyes, puffy lids.	Lid retraction, lid lag, chemosis, proptosis(exophthalmos) infiltrative ophthalmopathy, ocular muscle paresis, exposure keratopathy.
Skin	Thyroid acropathy, clubbing of fingers	Infiltrative dermopathy

CLINICAL FEATURES OF HYPOTHYROIDISIM

	Symptoms	Signs
General	Blunting of features, generalized slowing.	Periorbital puffiness, psychomotor retardation.
Skin	Dryness, itching	Dry, rough and flaky skin, non pitting oedema, carotenaemia.
Hair	Hair loss and thinning	Coarse and brittle hair, selective areas of alopecia.
CVS	Shortness of breath, angina pectoris, congestive cardiac failure.	Bradycardia, ischemic heart disease, pericardial effusion.
CNS	Muscle aches and pains, slowing of motor function, deafness, somnolence, loss of memory, decreased concentration	Delayed relaxation of tendon reflexes, myotonia and myxoedema, carpal tunnel syndrome, nerve conduction deafness, slowing of cerebration.
GIT	Constipation, weight gain	Ileus, ascites.
Reproductive System	Menstrual irregularities (usually menorrhagia), infertility galatorrhoea.	High FSH/ LH
Haematological System	Pallor, non-responsive anaemia, Bleeding tendencies.	Dimorphic anaemia, Megaloblastic anaemia, coagulation defects.
Miscellaneous	Cold intolerance, thick and coarse speech, fatigue, muscle-cramps, arthritis.	Hypothermia

Euthyroid ophthalmopathy

Accounts for less than 10% of patients with presumed thyroid disease. It provides a difficult diagnostic challenge. By definition, in euthyroid disease, base line thyroid function test are normal. So in these cases thyroid stimulating hormone levels should be measured for confirmation.

PATHOLOGY AND PATHOPHYSIOLOGY OF THYROID RELATED ORBITOPATHY

Graves' orbitopathy occurs in a generally pre-selected population, affecting females (usually middle aged), four to five times more frequently than males. The pathology of orbital involvement reflects the immuno-pathogenic mechanism. The major target affected is the extra-ocular muscles.

PATHOPHYSIOLOGY

The extra-ocular muscles are infiltrated by round cells i.e. lymphocytes, plasma cells and occasional mast cells. There is deposition of hydrophilic mucopolysacchrides, and the formation of collagen causes degenerative changes in the extra ocular muscles thus reflecting target effects of the disease on the orbital myocyte and the endomysial fibroblast. The plasma cells mediate the release of mucopolysaccharides and the formation of collagen by fibroblasts. There is usually a moderate inflammatory infiltration with plasma cells, lymphocytes and mast cells surrounding the blood vessels and muscle fibres. The muscle fibres appear distended and there is separation of the fibres by a loose, mucopolysaccharide rich stroma. With increasing severity and duration of inflammation, stromal collagen deposition occurs and muscle degeneration may be noted.

Ultimately the disease passes into a more quiescent stage, when the degenerated muscle tissue may be replaced by fat.

Orbital fibroblasts are susceptible to the action of pro-inflammatory cytokines.

IMMUNOLOGY

The immune system must be regarded as a homeostatic mechanism capable of responding to stimuli from the external environment and from the organism's internal milieu. In order to respond, the system must have anatomical components receiving, processing, integrating, and reacting to immunological challenges. The immune network includes the afferent and efferent divisions.

The Hypothesis put forth for the pathogenesis in the past

a. Warthin's concept of a thymico- lymphatic body, which is a consequence rather than a cause.

b. Hyper function of the anterior pituitary, with release of excess thyroid stimulating hormone (thyrotropin) is disproved. Since in primary myxoedema also thyroid stimulating hormone increases, but there is no exophthalmos.

c. Exophthalmos producing substances (EPS), distinct from thyrotropin.

The Site of Immuno-Pathology

Fibroblasts of the connective tissue stroma and basement membrane of the thyroid have been proven by immuno-fluorescent studies. As the target

cells in thyroid associated orbitopathy, sensitive to cytokines from lymphocytes.

(i) Clinical Evidence

Patients with any or all manifestations of Graves' disease have an increased incidence of other diseases known to have an immunologic basis. Thymic hyperplasia, lymphadenopathy and splenomegaly are findings often indicative of systemic immunological imbalance, may also be present.

The effectiveness of the following treatment modalities :

1. Systemic corticosteroids
2. Immuno suppressive agents e.g: cyclosporine and cyclophosphamide
3. Orbital irradiation

Supports an immunological basis for the manifestations of the Graves' disease.

(ii) Humoral Evidence – Long Acting thyroid Stimulator (LATS)

This substance was indeed shown to be an IgG immunoglobulin, but only 50-60% of Graves' thyrotoxic patients had detectable levels of LATS and, even when present, the LATS titre failed to correlate with either the thyroid or ophthalmic disease activity.

Thyroid – stimulating immunoglobulins (TSI) have now replaced LATS as the suspect humoral factor. These IgG immunoglobulins, undetected by the LATS assay, have been found in the sera of over 90% of Graves' thyrotoxic patients. Immune complexes are combinations of antibody and antigen. Immune complex binding to extra ocular muscle significantly exceeds binding affinity for other tissues.

(iii) Cellular Evidence

The diffuse lymphocytic infiltration of orbital tissues that characterize Graves ophthalmopathy, and the high incidence of concurrent thymic abnormalities have logically led to investigation of the cellular immune system. Lymphocytes from patients with Grave's disease had statistically significant migration inhibition factor (MIF) titres compared to lymphocytes from normal controls.

In Caucasian patients with this "disorder", an increased frequency of HLA-B8 has been reported. When a population of Japanese patients were investigated an increased incidence of HLA – BW 35 antigen was found. HLA – Cw3 and HLA – DR3 have also been reported to be associated with Grave's disease.

Pro-Inflammatory Cytokines:

The following two cytokines production are increased in orbital fibroblasts

1. PG HS2: An inflammatory cyclo oxygenase, which in turn increases production of PGE2.

2. PGE2: The production of both is up regulated in the orbital fibroblasts and can be blocked by gluco-corticoids.

The extra ocular muscles and peri-orbital connective tissue accumulate non-sulfated glycosaminoglycans – hyaluronan, accompanied by intense autoimmune inflammation. There is a doubling of the hyaluronic acid content in the orbital tissue which results in a five fold increase in the tissue osmotic load. The osmotic damage causes muscle oedema and proptosis. Subsequent fibrosis of muscle fibres and eventual tissue atrophy ensues. Active inflammation in the acute and sub- acute stages progresses to the quiescent stage and results in fibrosis.

THYROID EYE DISEASE

The onset, course, severity and relationship to the systemic disease is variable. Grave's orbitopathy usually occurs in association with hyperthyroidism but some patients with typical features of Grave's orbitopathy may be hypothyroid or even euthyroid.

CLINICAL FEATURES

There are two stages in the development of the disease:

1. Stage of Active Inflammation

Where the eyes are red and painful. It usually remits within three years but 10% of the patients develop serious long-term ocular problems.

2. Quiescent Stage

Where the eyes are white but painless motility defects are present. The five main clinical manifestations of *dysthyroid ophthalmopathy* are

1. Eyelid retraction
2. Soft tissue involvement
3. Proptosis
4. Optic neuropathy
5. Restrictive myopathy

EYELID RETRACTION

The normal position of the upper lid is 1-2mm below the upper limbus. Lid retraction leads to a characteristic starring appearance.

Postulated mechanisms

a. Contraction of the levator associated with fibrosis and local adhesions between levator and overlying orbital tissues. In the lower lid, fibrosis of the inferior rectus muscle may induce retraction via its capsulopalpebral head.

b. Secondary overaction of levator – superior rectus complex in response to the hypohoria produced by fibrosis and tethering of the inferior rectus muscle *(manifested by increased lid lag on shifting from down gaze to up gaze).* Retraction of lower lid resulting from overaction of inferior rectus may also occur secondary to fibrosis of superior rectus muscle.

c. Chemically induced overaction of Muller's muscle as a result of sympathetic overstimulation secondary to high levels of thyroid hormone.

In general, lid retraction is thought to be due to a sympathomimetic response in the early stages, whereas in the later stages it may be associated with fibrosis of lid tissues.

Signs and Symptoms of Soft Tissue Involvement

Symptoms – Excessive lacrimation, gritty sensation, discomfort and photophobia.

Signs

a. ***Conjunctival Injection***

b. ***Chemosis***

c. ***Edema and Fullness of the Lids***

These often coexist, though sometimes oedema may be present without fullness. Lid fullness reflects oedema and infiltration behind the orbital septum whereas lid oedema alone is the result of fluid anterior to the orbital septum, just under the skin and orbicularis muscle. Periobital puffiness, usually worse in the mornings, is often the result of prolapse of retro-orbital fat into the lids.

d. ***Superior Limbic Keratoconjunctivitis*** is a sensitive sign of soft tissue involvement

Proptosis is a characteristic finding, seen in about 60% of the patients. The onset is usually insidious, and progression is gradual. Proptosis is typically axial and it occurs due to several causes.

a. Enlargement of extra ocular muscle. Small changes in orbital volume may cause a significant increase in protosis.

b. Increased orbital fat volume with or without muscle involvement.

c. Venous stasis due to increased orbital pressure. Enlargement of superior rectus muscle alone may compress the Superior Ophthalmic Vein, resulting in reduced venous outflow from the orbit, thereby increasing the apparent orbital fat volume.

Complications

Exposure Keratitis

This results from:

- Inadequate lid closure due to proptosis and lid dysfunction.
- Loss of the protective Bell's phenomenon in patients with restrictive myopathy.

Visual Loss

This is an important but rare complication of thyroid eye disease. It can be caused by:

- Dysthyroid optic neuropathy
- Exposure keratopathy, with subsequent corneal ulceration and opacification or perforation with panophthalmitis and loss of the eye.

Dysthyroid Optic Neuropathy

The incidence of optic neuropathy in thyroid disease is approximately 5% and affected individuals usually do not have marked proptosis or optic nerve changes on ophthalmoscopy. The following are the signs and symptoms of this condition.

Symptoms

a. Ophthalmoscopic evidence of disc oedema or pallor
b. Visual field defects
c. Afferent papillary defect

The neuropathy is probably caused by mechanical compression of the optic nerve. Examination of the ophthalmopathy patient with suspected optic neuropathy should include visual acuity, colour vision, pupillary examination for afferent pupillary defect, funduscopy, and visual field examination by perimetry. The most common visual field defects, paracentral scotomas, and generalized constriction of the visual field.

***Restrictive Thyroid Myopathy* –** Between 30 –50% of hyperthyroid patients develop ophthalmoplegia. Ocular motility is restricted by oedema in the infiltrative phase and by fibrosis in the fibrotic phase. Typically, there is first a limitation of elevation followed later by a limitation of abduction, usually associated with diplopia in the corresponding fields of gaze. Most thyroid ophthalmopathy patients, including those with no ocular motility symptoms, show some degree of extra ocular muscle involvement by ultra-sonography.

CLASSIFICATION

Eponymic Eye Signs in Graves' Disease

Lid Signs

Upper Lid

1. Boston's sign – Uneven jerky motion of upper lid on inferior movement.
2. Dalrymple's sign – Upper lid retraction.
3. Gifford's sign – Difficult eversion of upper lid.
4. Jellinek's sign – Abnormal pigmentation of upper lid.
5. Kocher's sign – Spasmodic retraction of upper lid during fixation with staring look and frightening appearance of eyes.
6. Von Graefe's sign – Upper lid lag on downgaze.

Lower Lid

1. Enroth's sign – Oedema of lower lid.
2. Griffith's sign – Lower lid lag on upgaze.

Both Upper and Lower lids

1. Rosenbach's sign – Tremor of gently closed lids.
2. Vigouroux's sign – Puffiness of lids.
3. Riesman's sign – Bruit over eyelids.

On Upgaze

1. Joffroy's sign – Absent creases in forehead on superior gaze
2. Mean's sign – Increased superior scleral show on upgaze (Globe lag)
3. Sainton's sign – Frontalis contraction after cessation of levator activity

On Downgaze

1. Boston's sign – as above
2. Von Graefe's sign – as above

Motility and Extra Ocular Muscles

1. Ballet's sign – Paralysis of one or more extra ocular muscles
2. Moebius sign – difficult convergence
3. Suker's sign – Inability to maintain fixation on extreme lateral gaze
4. Wilder's sign – Jerking of eyes on movement from abduction to adduction

Pupillary Signs

1. Cowen's sign – Extensive hippos of consensual pupillary light reflex
2. Knies' sign – Uneven pupillary dilatation in dim light
3. Loewi's sign – Dilatation of pupil with 1:1000 epinephrine

On Blinking

1. Pochin's sign – Reduced amplitude of blinking
2. Stellwag's sign – Incomplete and infrequent blinkingOthers

1. Goldzieher's sign – Deep injection of conjunctiva, especially temporally
2. Payne – Trousseau's sign – Dislocation of the globe
3. Riesman's sign – as above
4. Snellen – Donder's sign – Bruit over eye

The original classification for thyroid eye disease was given by **Werner** as Chair of the American Thyroid Association adhoc sub committee on eye disease-**NO SPECS.** Subsequently modified by American Thyroid Association (ATA) in 1997.

Classification of Eye Changes of Grave's Disease – Werner's NOSPECS

Class	Grade	Suggestion for Grading
0	**No physical signs or symptoms**	
I	**Only signs – limited to upper lid retraction, lid lag**	
II	**Soft Tissue involvement with symptoms and signs**	
	0	- Absent
	A	- Minimal
	B	- Moderate
	C	- Marked
III	**Proptosis**	
	0	- Absent
	A	- 3-4 mm increase over upper normal
	B	- 5-7 mm increase over upper normal
	C	- 8 mm or more increase
IV	**EOM Involvement**	
	0	- Absent
	A	- Limitation of motion at extremes of gaze
	B	- Evident restriction of motion
	C	- Fixation of globe or globes

V	**Corneal Involvement**	
	0	- Absent
	A	- Stippling of cornea
	B	- Ulceration
	C	- Clouding, necrosis, perforation
VI	**Sight Loss Caused by Optic Nerve Involvement**	
	0	- Absent
	A	- Disc pallor or chocking or visual field defect; vision 20/20 – 20/60 (6/6 – 6/18)
	B	- Vision 20/80 – 20/200 (6/24 – 6/60)
	C	- Vision <20/200 (<6/60) (blindness – failure to perceive light)

The first letter of each class in the grading system spells the mnemonic NO SPECS. As shown in this table, each class in divided into four grades: absent (0), mild (a), moderate (b), and marked (c).

Van Dyk proposed an expansion of Werner's class II soft tissue changes with the mnemonic **R E L I E F**.

R – Resistance to retro displacement of the eye.

E – Edema of the conjunctiva

L – Lacrimal gland enlargement

I – Injection of conjunctiva

E – Edema of lids

F – Fullness of lids

The classification systems are intended to reflect the degree of severity of thyroid eye disease but do not indicate the course of disease progression.

There are two major clinical groups:

1. Non-Infiltrative Orbitopathy

90% of cases fall under this category. This is the mild variety and is classified as class 0 or 1 in Werner's NOSPECS classification.

2. Infiltrative Disease

Classes 2 through 6 have infiltrative disease and accounts for 10% of all cases of Grave's hyperthyroidism. These patients have a more fulminant course with significant infiltration, inflammation and scarring.

Thus Werner's classification allows us to record the clinical status of a patient but does not reflect a continuum of disease or progression in an individual patient.

Course of the disease

Thyroid opthalmopathy is typically a self-limited process that becomes quiescent within 3 to 5 years of its onset. Spontaneous remissions and exacerbations have been reported in thyroid opthalmopathy in the pre-treatment era.

- Eyelid retraction may improve in upto 50% of the patients.
- Proptosis usually remains stable once it reaches its maximum.
- Ocular motility can also vary with time, and unless vision is threatened, patients should be followed up for periods of upto 6 months to ensure stability before therapeutic intervention.
- Visual loss – As many as 10% of patients with thyroid eye disease develop severe, vision threatening ophthalmopathy. Patients with optic neuropathy may show spontaneous improvement. In one analysis of 32 untreated eyes, 19% had final visual acuity ranging from counting fingers to no light perception.

LABORATORY EVALUATION

1. TSH (Thyroid Stimulating Hormone)

a. The most useful and most sensitive initial thyroid function test especially for screening outpatients. Sub – clinical disease is detected earlier with serum thyroid stimulating hormone than with conventional hormone studies. In addition thyroid stimulating hormone levels are not affected by alteration in thyroid – binding proteins.

It is useful in following patients receiving thyroid hormone therapy.

i. Sub clinical hypothyroidism - elevated

ii. Hyperthyroidism - suppressed

iii. Euthyroid ophthalmopathy - decreased level in the presence of normal levels of T_3 and T_4

- The Immune radio immunoassay method can measure very low levels of serum thyroid stimulating hormone and hence a very sensitive test.

b. Elevated basal thyroid stimulating hormone levels with successive response to thyroid releasing hormone indicates primary hypothyroidism.

- Absence of thyroid stimulating hormone response to thyroid releasing hormone with low T_3, T_4 and thyroid stimulating hormone – pituitary deficiency.

- Partial or normal response of thyroid stimulating hormone to thyroid releasing hormone secretion.

2. Serum T_3 and T_4 levels

Total serum T_3 and T_4 levels and the Thyroid Hormone – Binding Ratio (THBR), which is measured as T_3 resin uptake. This T_3 resin uptake test helps indirectly measure serum free T_4. Both hormones exist in free and bound forms. The amount of free hormone is influenced by changes in serum protein binding. Serum free T_4 is estimated by multiplying the total serum T_4 by the thyroid hormone binding ratio. The total T_4, thyroid hormone binding ratio and free T_4 values may be altered with primary thyroid disease and with changes in serum thyroid – binding proteins. In hyperthyroidism – all are increased. The rise in T_3 is proportionately more than T_4. In hypothyroidism serum levels of T_4 are low and serum T_3 is variable. Free T_4 is more reliable, as it avoids the interfering effects of varying thyroxine binding globulin levels. Free hormone levels are more sensitive as they are not vulnerable to levels of thyroxine binding globulin.

3. Thyroid Antibody Tests

Thyroid stimulating Antibody (**TSAb**) test is available only in research laboratories and is important for

a. Establishing immunological aetiology

b. Normal value on follow up ascertains a state of complete remission.

c. Diagnosis of Grave's disease and euthyroid Grave's ophthalmology.

- If there is significant thyroid stimulating antibody titre, only reversible measure for control of hyperthyroid state should be employed. Antimicrosomal antibodies are present in patients with Hashimoto's disease and to a lesser extent in patients with Grave's disease. Hence indicated in possible

  i. Sub-clinical hypothroidism

  ii. Hashimoto's disease suspects where the thyroid stimulating hormone level and anti-microsomal antibody levels are elevated.

RADIO IODINE UPTAKE SCAN

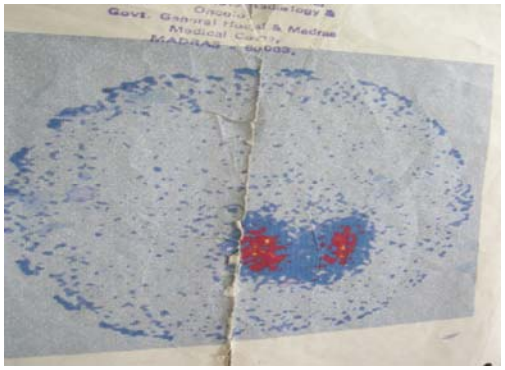
^{131}I uptake – measured after 2 hours and after 24 hours. The beta rays emitted along with few gamma rays is measured by a Geiger Muller counter. Increased uptake occurs in hyperthyroidism. If associated with T_3 suppression, will determine whether the gland is autonomous or not. No more use nowadays.

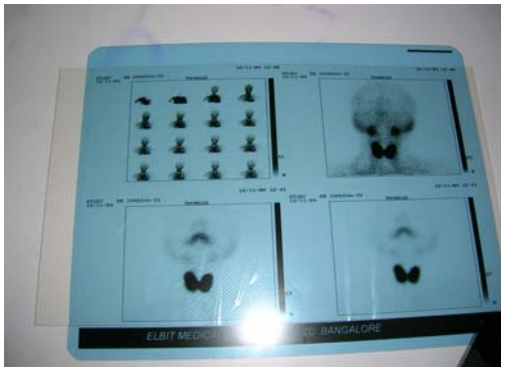
For Hyperthyroidism

1. Free hormone and thyroid stimulating hormone levels in blood.
2. Thyroid Stimulating Antibody (TSAb) for immunologic basis for Grave's disease.
3. Assessment of end organ involvement.
4. Nuclear scanning.

Measurement of basal thyroid stimulating hormone level by radioimmunoassay method provides the most reliable first line test. T_3 and T_4 levels are raised; the rise in T_3 is proportionately more than in T_4. Sometimes, only T_3 may be raised while T_4 is in normal range (T_3 thyrotoxicosis). Free hormone levels are more sensitive as they are not vulnerable to levels of thyroxine binding globulin. Thyroid stimulating hormone is absent or hardly detectable in patients with thyrotoxicosis.

RADIO IODINE UPTAKE SCAN





For Hypothyroidism

The diagnosis of hypothyroidism can be confirmed by:

1. Level of thyroid hormone in circulation.

2. Value of thyroid stimulating hormone and its response to thyroid releasing hormone.

3. Indirect tests like serum enzymes (creatine phosphokinase, lactate dehydrogenase) and electrocardiogram.

4. Thyroid antibody tests.

5. Others like basal metabolic rate, serum Cholesterol, protein bound Iodine, radioactive Iodine 131 uptake tests are not of much use in the presence of the more useful tests listed above.

Thyroid stimulating hormone is the most sensitive test for detection or confirmation of sub clinical or overt hypothyroidism.

Normal Serum Values

Serum T_3	(0.8 to 2.0 ng/ml)
Serum T_4	(4 to 12 μg/dl)
Serum TSH	(0.5 to 4.5 μIU/ml)

IMAGING IN THYROID RELATED ORBITOPATHY

1. Ultrasonography in Thyroid Related Orbitopathy

The Ultra-sonography can demonstrate subtle changes occurring in extra ocular muscle and orbital fat. These changes are reflected in an irregular posterior outline of the retro-bulbar fat pattern, quantifiable enlargement of the extra ocular muscles and accentuation of the orbital walls. The enlarged muscles show intra muscular echoes due to separation of the muscle bundles. Optic neuropathy may be associated with expansion and reduplication of the distal portion of the nerve sheath due to expansion of the sub-arachnoids space. A scan demonstrates high acoustic reflectively in the muscle bellies due to separation of the muscle fibres.

2. Computed Tomography in Thyroid Related Orbitopathy

About 90% of patients with thyroid orbitopathy will have bilateral computed tomography abnormalities, even if the clinical involvement is unilateral. Relatively symmetrical computed tomography findings are seen in 60% to 70% of patients and any of the extra ocular muscles can be involved.

Inferior rectus > **Medical rectus** > **Superior rectus** > **lateral rectus**.

This parallels clinical oculomotor manifestations.

Typically the muscle enlargement involves the muscle belly from the annulus to the origin of the tendon, and so occurs primarily behind the posterior margin of the globe. There are low densities seen within the muscle bellies. These areas represent lymphorrhages (focal accumulation of lymphocytes or mucopolysaccharide deposition. With long standing disease, larger low-density areas may appear in the muscle, probably representing fatty replacement.

Apical crowding and reduced space around the posterior portion of the optic nerve with sharp angulation of the posterior belly of the muscle indicates optic neuropathy.

Coca-cola sign i.e. medial bowing of the medial orbital wall with reduction in size of the adjacent ethmoid sinuses. Forward displacement of the globe and slight engorgement of the lacrimal gland. Tenting of the posterior globe may be due to traction on the globe.

3. MRI – Non Ionising radiation

Delineation of compressive optic neuropathy is easier with MRI than CT.

MANAGEMENT

Management should consist of a co-ordinated multi-disciplinary, medico-surgical approach, based on clinical patho-physiologic inference, staging of the disease and knowledge of its effects on the orbital and ocular structures. Broadly speaking, management is directed towards abatement or the control of inflammation, prevention of ocular and psycho visual damage, redressing ocular motor abnormalities, and improving cosmetic disfigurement.

Managing Graves' Orbitopathy

Unless there is an immediate threat to vision, surgical treatment should be postponed until the active phase of the disease subsides so as to avoid surgical over correction. Sight threatening corneal exposure or optic neuropathy may require immediate surgical intervention regardless of the state of the disease.

Treatment of Hyper Thyroidism

Anti-thyroid drugs – The first-line treatment for hyperthyroidism is with Thioimidazole. These reduce systemic symptoms but their benefit with regard to Grave's orbitopathy is questionable.

Oral Radioactive Iodine Therapy – Many patients become hypothyroid within several years after this treatment and require thyroid

hormone replacement. Increased incidence of ocular symptoms after radioactive iodine therapy has been reported after (^{131}I) (Iodine 131) thus either subsequent development or exacerbation of Grave's ophthalmopathy.

Surgical Thyroidectomy – It is reserved for patients whose disease cannot be controlled with medical treatment or for those who will not tolerate or accept radioablation. Some studies show that Thyroidectomy stabilized or improved signs of endocrine ophthalmopathy. Subtotal thyroidectomy also showed significant improvement in proptosis and in muscle diameter in contrast to those treated with radioiodine.

Medical Management of Orbitopathy

Steroid Treatment

These agents probably serve in multiple capacities by suppressing immune function and decreasing inflammation, but though the beneficial effects are clear the exact mechanism is far from clear.

Indications:

a. For any patient with evidence of optic neuropathy, in addition he may require radiation or orbital decompression.

b. For patients with acute orbital inflammation a course of systemic steroids will decrease chemosis, injection and proptosis within

days. However, some patients require long-term steroid use to prevent exacerbation of symptoms. 60 to 100 mg of prednisone per day for several days, followed by a slow taper by 5 to 10 mg over the subsequent weeks.

Two – thirds of patients will respond to the above regimen regardless of their age, gender or severity of the eye disease. However, chronic, stable Graves' orbitopathy does not respond to steroids or radiation. It is advisable to limit the use of steroids to a few months duration, to prevent the numerous side effects associated with long-term steroid use. Supplementation with immune suppressive therapy or radiotherapy should be considered in the event of extended treatment being required.

Immunosuppressive Therapy – Immunosuppressive agents like cyclosporine, cyclophosphamide, methotrexate and azathioprine are reserved for rare patients who fail or cannot undergo standard treatment with steroids, radiation or surgery. Due to the toxicity associated with this type of immuno suppressive therapy the use of these medications has largely reduced.

Orbital Irradiation – Steroids and local orbital irradiation have similar effects or Grave's orbitopathy and it is unusual for radiation to succeed if steroids have not. Radiation typically has no effect on chronic stable Grave's orbitopathy. Dose – 2000 cGy total dose in small fractions, over a period of 2 weeks to minimize the undesirable side effects.

Surgical Management – Multiple surgical procedures involving the orbit, muscles and eye lids are often required to correct the functional consequences of Grave's ophthalmopathy. An optimal result is likely if the disease has been quiescent for at least 6 months.

Sequence of surgery – orbital decompression, prior to strabismus surgery and finally eyelid surgery.

Surgeries are mainly to decrease the Exophthalmous or to decrease the starring look due to lid retraction. There are newer modalities for treating lid retraction like 'Z' Myotomy which gives a good cosmetic result especially in female patients.

Part - II

AIM OF THE STUDY

To study in detail about various presentations of thyroid Related orbitopathy with special reference to lid retraction and its management (Z - MYOTOMY)

MATERIALS AND METHODS

Thyroid orbitopathy was diagnosed in 30 patients who attended Regional Institute of Ophthalomology and Government Ophthalmic Hospital between May 2004 and August 2005 and they were subjected for detailed study.

Inclusion Criteria

1. Patients with proptosis of thyroid origin
2. Patients with lid retraction.

Exclusion Criteria

1. Patients with multiple endocrine abnormalities were not included in the study.
2. Patients with proptosis due to cystic lesions were not included.
3. Patients with suspicious malignant thyroid disease were not included.
4. Bilateral proptosis due to any other cause.

Patients Evaluation

All patients who were included in the study were worked up in the following manner

1. Detailed History with reference to the

- duration of illness
- onset
- Rate of progression of proptosis
- presence of progressive lid refraction
- prior medical treatement or surgical treatment
- any other associated symptoms.

2. Complete ocular examination

- Visual acuity by Snellen's chart
- Examination of orbit and eyelids.
- Examination of eye for IOP with Schiotz tonometry,
- Special emphasis on Hertels exophthalmometer.
- Hess screen
- Extra Ocular Movements
- Colour vision.
- Field of vision.

3. Thyroid status evaluation which included

- Thyroid function tests from endocrinology Department
- Radiological investigations like X-ray orbit and CT scan
- USG neck for thyroid mass
- 'B' scan for EOM enlargement / to ruled out optic nerve compression.
- Radio iodine uptake study using I^{131} (or) Tc 99m Pertechnetate
- FNAC / Biopsy of the thyroid gland.

One or more thyroid evaluation tests were done as per the individual case assessment. Results of thyroid function tests were obtained from Govt. General Hospital Endocrinology Department.

Patients were also referred to other departments like ENT, OBS/GYNAEC, MEDICAL / SURGICAL OP and ENDOCRINOLOGY to get expert opinion regarding diagnosis and management whenever indicated.

ANALYSIS AND DISCUSSIONS

Total numbers of 30 cases reported to our hospital with thyroid eye disease were studied. Their clinical profiles were analysed for the following parameters.

a. Age Incidence

Range	No. of Cases	Percentage
16 – 20 yrs	2	6.6%
21 – 30 yrs	9	30%
31 – 40 yrs	14	46.6%
41 – 50 yrs	3	10%
51 – 60 yrs	2	6.6%

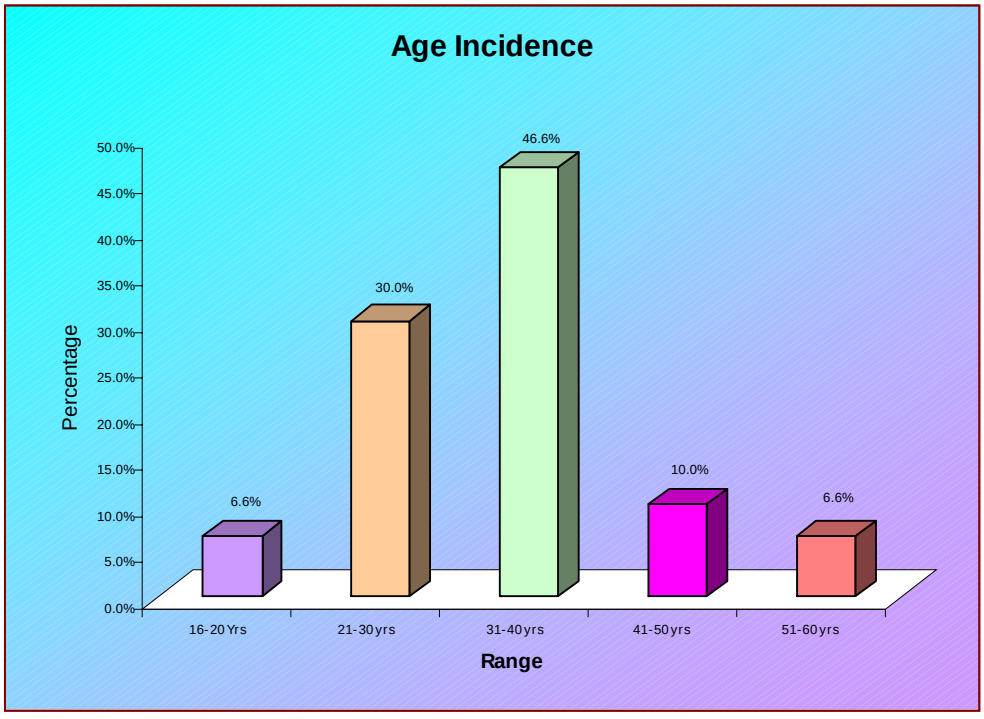
Age incidence varies from 16 – 60 years with highest no. of cases falling between 31 – 40 yrs. (J^{10})

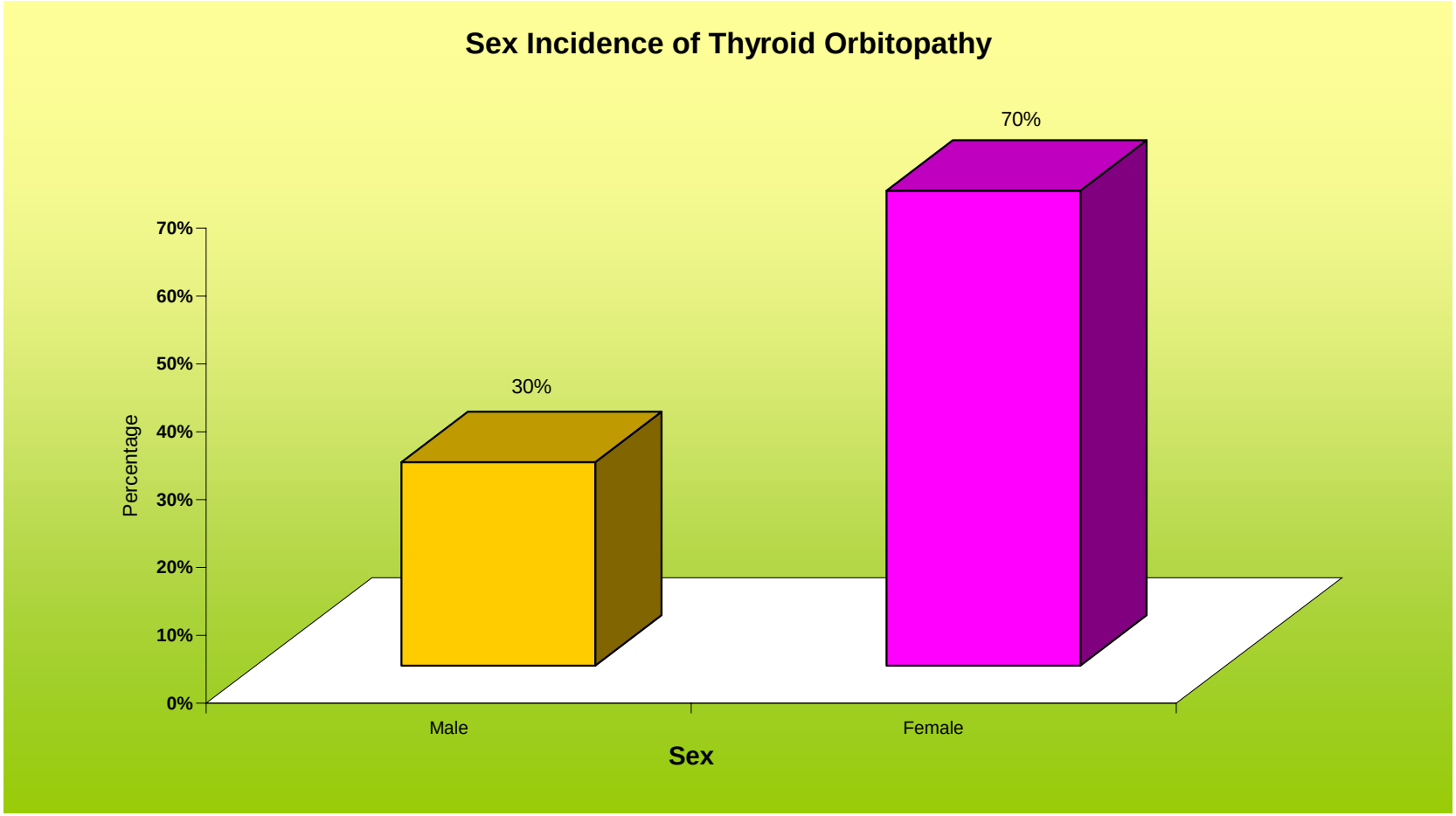
b. Sex Incidence of Thyroid Orbitopathy.

Sex	Number of cases	Percentage
M	9	30%
F	21	70%

In our study, a female preponderance (70%) was seen as expected in any thyroid problem. (11).

16 YEARS - 60 YEARS




Sex Incidence of Thyroid Orbitopathy
70%
30%
70%
60%
50%
40%
30%
20%
10%
0%
Percentage
Male
Female
Sex

c. Laterality of Proptosis

Bilateral	14	63.6%
Unilateral	8	36.3%

Bilaterality was reported in more than 50% of cases with proptosis confirming to the norms of thyroid eye disease.

d. Direction of Proptosis

Type	Number of Cases	Percentage
Axial	21	70%
Eccentric	1	3.3%
No proptosis	8	26.66%

In our study axial displacement of the Globe was more common (70%) (J^5)

e. Complaints

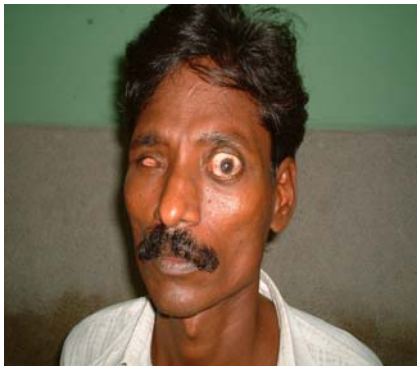
Complaints	No. of cases
Protrusion	18
Watering	15
Retrobulbar Discomfort	15

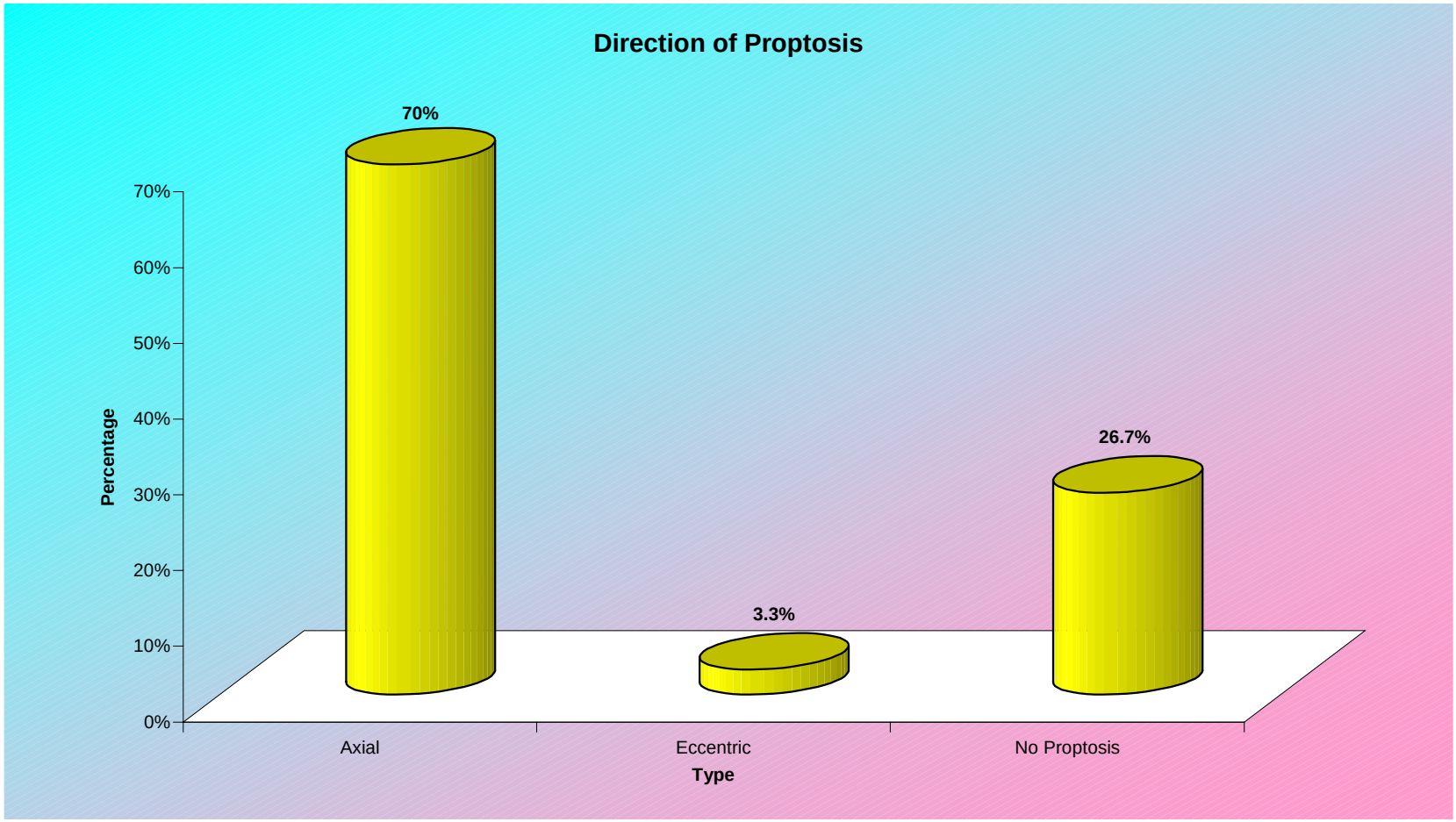
Majority of patients complained of watering and RB discomfort (J^5) in addition to proptosis.

PROPTOSIS

BILATERAL

UNILATERAL




Direction of Proptosis
70%
3.3%
26.7%
70%
60%
50%
40%
30%
20%
10%
0%
Percentage
Axial
Eccentric
No Proptosis
Type

f. Toxic Symtoms

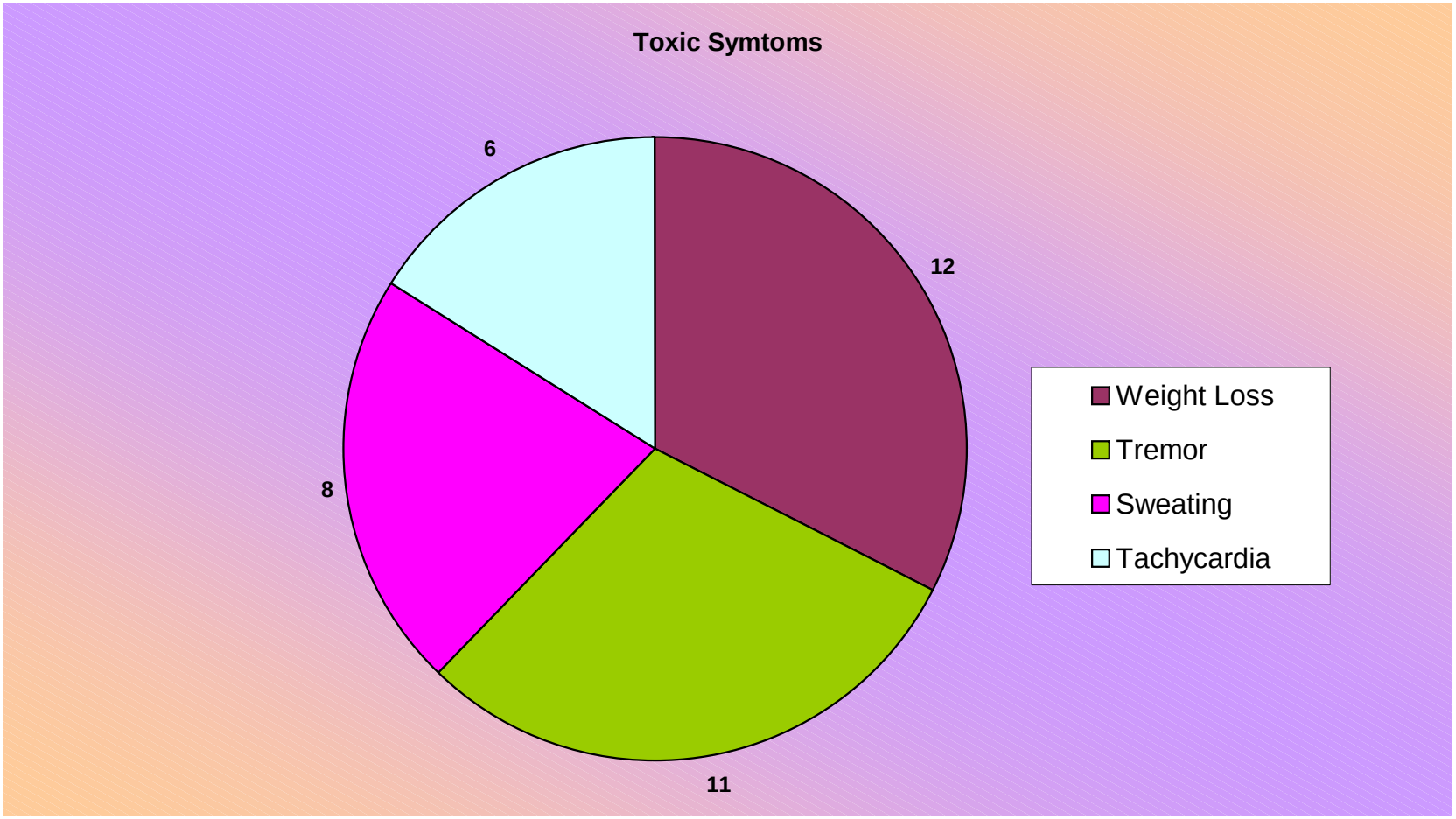
Symptoms	No. of patients
Weight loss	12
Tremor	11
Sweating	8
Tachycardia	6

The symptoms of thyrotoxicosis were elicited from patients and many of them had one or more major toxic symptoms.

g. Lid Signs

Though lid signs in thyroid are many and varied, the most important and frequently appearing lid signs in the order of frequency of occurrence are enumerated here.

Lid signs	No. of cases with Bilateral presentation	Cases with unilateral presentation
Dalrymple sign	10	9
Vongrafe's sign	12	6
Kochers sign	8	8
Stellwag sign	6	6
Rosenbach sign	2	2


Toxic Symtoms
6
12
8
11
Weight Loss
Tremor
Sweating
Tachycardia

LID SIGNS

Von Graefe Sign

Griffith Sign

Kocher Sign

Dalrymple Sign

h. Visual Acuity

Vision	RE	LE
6/6 – 6/18	26	26
6/18 – 6/60	2	1
Less than 6/60	2	3

In our study, thyroid disease did not cause any visual disability and no case of compressive optic neuropathy was detected.

No abnormality was noted in tonometry, pupillary reaction, ophthalmoscopy, field charting and colour vision.

i. Exophthalmometry

Proptosis Grade	Numerical Value	No. of eyes	Percentage
Normal	<20	18	30%
Mild	21 – 23	34	56.66%
Moderate	24 – 27	8	13.33%
Severe	>27		

Majority of patients were found to have mild proptosis (56.66%)

HERTEL'S EXOPHTHALMOMETRY

j. Nature of Thyroid swelling

Nature of Thyroid swelling	No. of patients	Percentage
Diffuse	18	60%
Nodular	6	20%
Multi-nodular	4	13.33%
No swelling	2	6.6%

In my study, associated thyroid swelling was present in almost all cases the details of which and given in the tabular column above.

k. Thyroid function Tests.

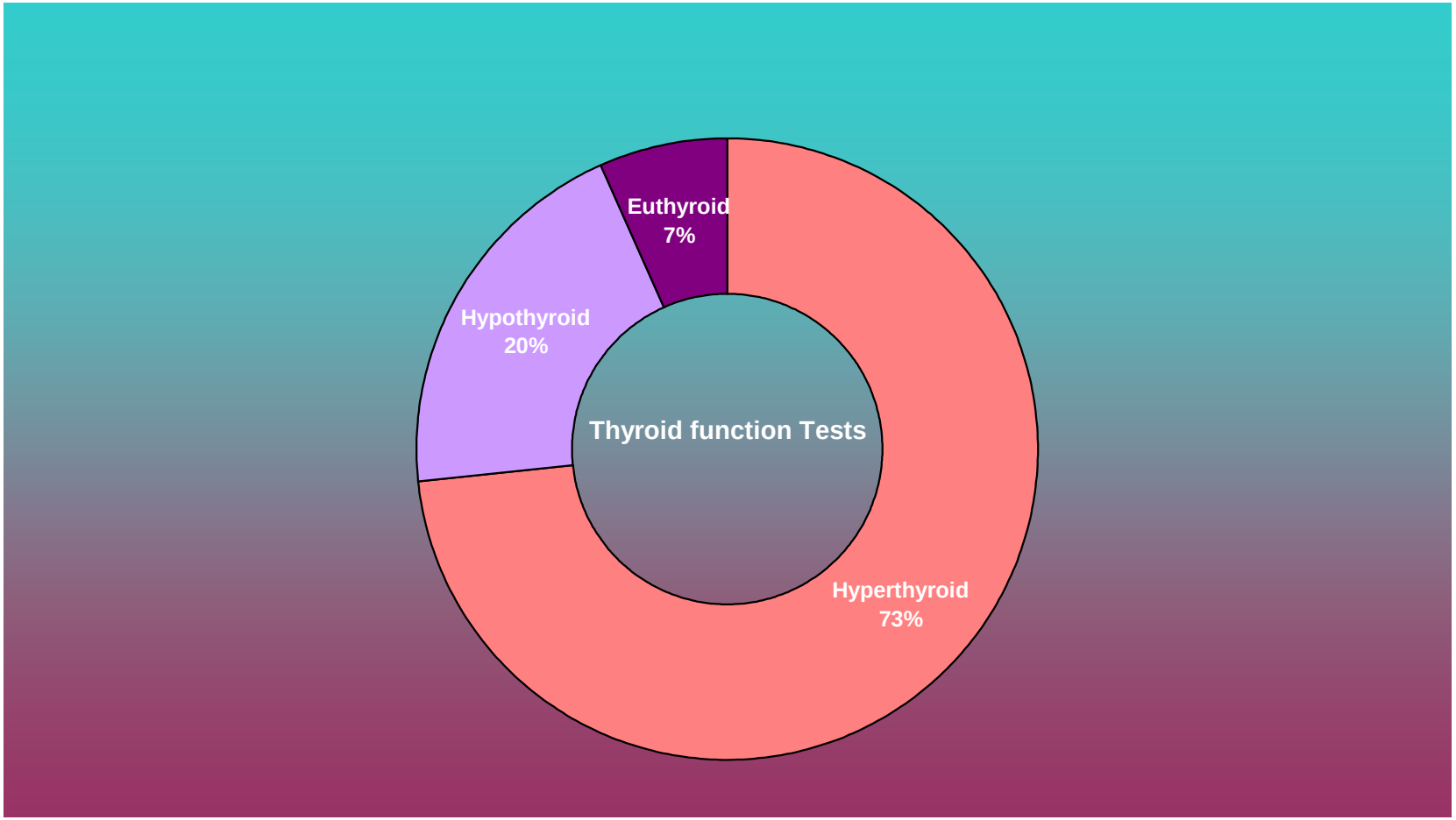
	T3	T4	TSH	%	
Increased	22	22	6	73.33%	Hyperthyroid
Decreased	6	6	22	20%	Hypothyroid
(N) Euthyroid	2	2	2	6.6%	Euthyroid

In my study hyperthyroid state was strongly associated with thyroid orbitopathy as shown above; this correlated with the ($J^{2,}$ J^{8})

NATURE OF THYROID SWELLING

MULTINODULAR

NO SWELLING


Euthyroid
7%
Hypothyroid
20%
Thyroid function Tests
Hyperthyroid
73%

l. Radio Iodine Uptake Scan

No. of cases	Alpha	Beta	Gamma
9	7	2	-----

Thyroid uptake scan showed

1. Hot nodules -- (α)in 7 cases
2. Warm nodules -- (β) in 2 cases
3. Cold nodules -- (γ) Nil

Which indicates hyperthyroidism is most commonly associated with thyroid orbitopathy.

m. USG orbit – 'B' Scan

No. of cases	Muscle Thickening	No Muscle Thickening
30	12	18
%	40%	60%

B Scan showed thickening of muscle bellies in 40 % cases.(**7**)

n. CT Scan – orbit

No. of cases	EOM Enlargement	Normal Study
11	10	1

CT scan is the study of choice in thyroid Related orbitopathy (J^1) but only 11 of my patients could afford CT scan.

o. Fine Needle Aspiration Cytology of Thyroid Gland

FNAC was done for 3 patients

Features suggestive of Hyperthyroidism	2
Features suggestive of Normal Thyroid Gland	1

Out of 3 cases with suspicion of malignancy with TNG, FNAC result was negative (FNAC was done by Department of Surgery) at Government General Hospital.

TREATMENT OF THROID

1. Medical Treatment:

Antithyroid Drugs	Eltroxin
20	6

2. Radio ablation for 1 patient was given at Nuclear Medicine Department Government General Hospital.

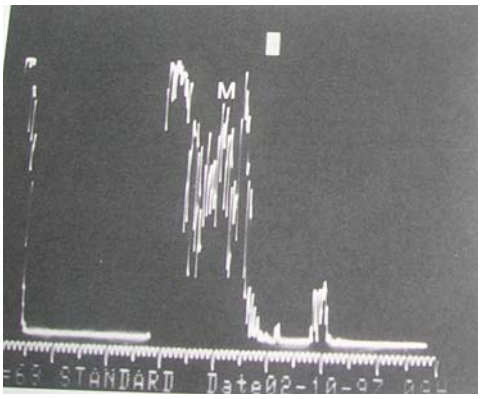
3. 2 patients have undergone thyroidectomy for hyperthyroidism at Govt. General hospital few years back.

Majority of my patients (twenty) were treated with antithyroid drugs and six of them were treated with thyroxine.

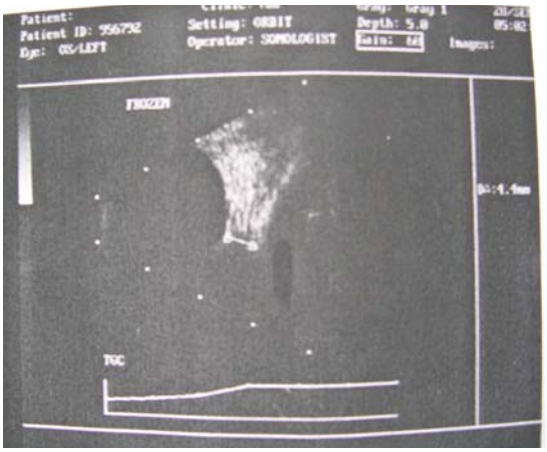
RADIO IODINE UPTAKE

'B' SCAN

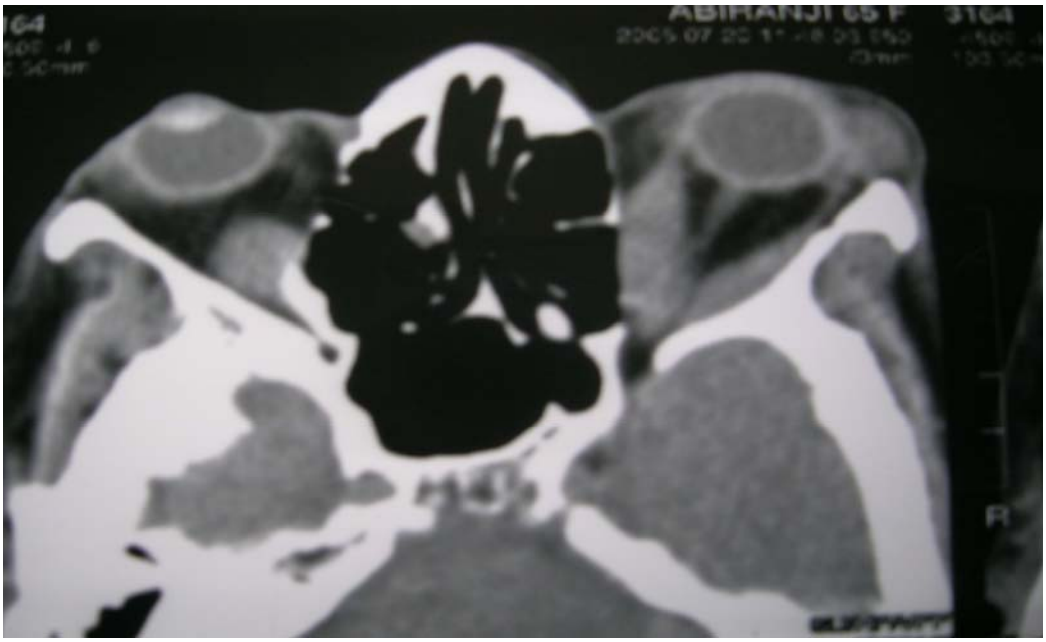

Patient:
Patient ID: 974295
Eye: OD/RIGHT
Setting: ORBIT
Operator: SONOLOGIST
Depth: 5.0
Gain: 62
Images:
FROZEN
Dual
FROZEN
OD LPS-SR
OS LPS-SR


M
STANDARD


M


Patient:
Patient ID: 356732
Eye: OS/LEFT
Setting: ORBIT
Operator: SONOLOGIST
Depth: 5.0
Images:
FROZEN
TOC

CT SCAN - ORBIT



OCULAR TREATMENT

Lubricating Drops	Oral steroids	Immunosuppressants
30	19	1

In my study simple conservative measures like lubricating drops was applicable to all my 30 patients (J^5). All my male patients were advised to stop smoking as it is known to aggravate the condition (J^9).

19 patients were treated with oral prednisolone and they showed good response with decreased (or) static exophthalmous[11].

Immunosuppressants are reserved for those not responding to steroids because of its toxicity[11] (J^2).

In my study it was started for a single patient but unfortunately the patient was lost for follow up.

As it was reported literature (J^7) patients not responding to steroids show poor response to radiotherapy. It was not tried for steroid, unresponsive patients.

Orbital decompression is indicated for compressive optic neuropathy and for disfiguring exophthalmos[11] (J^2) in thyroid related orbitopathy which was not noted in any of our cases.

SURGERY

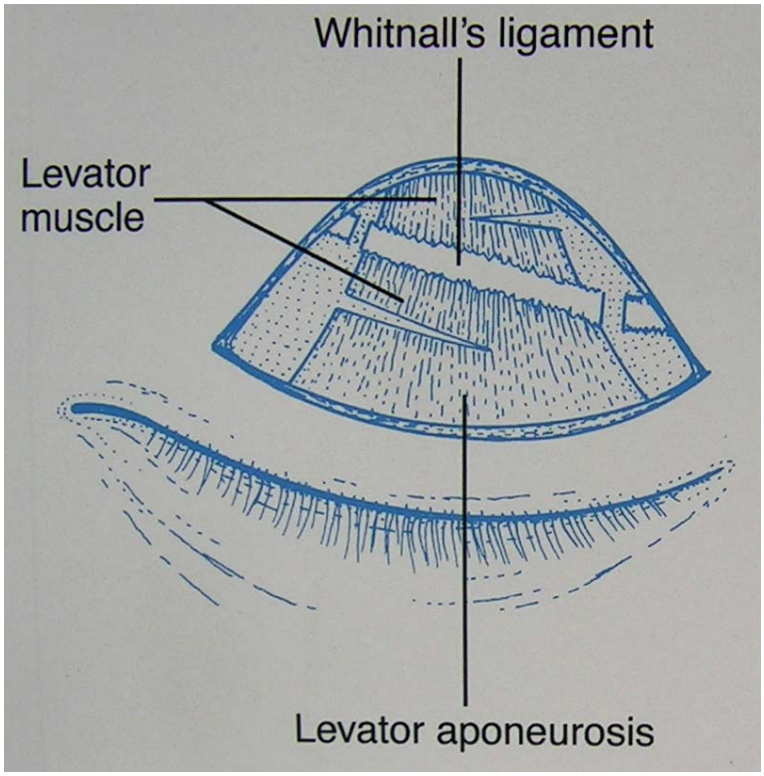
Cosmetic Eyelid Surgery

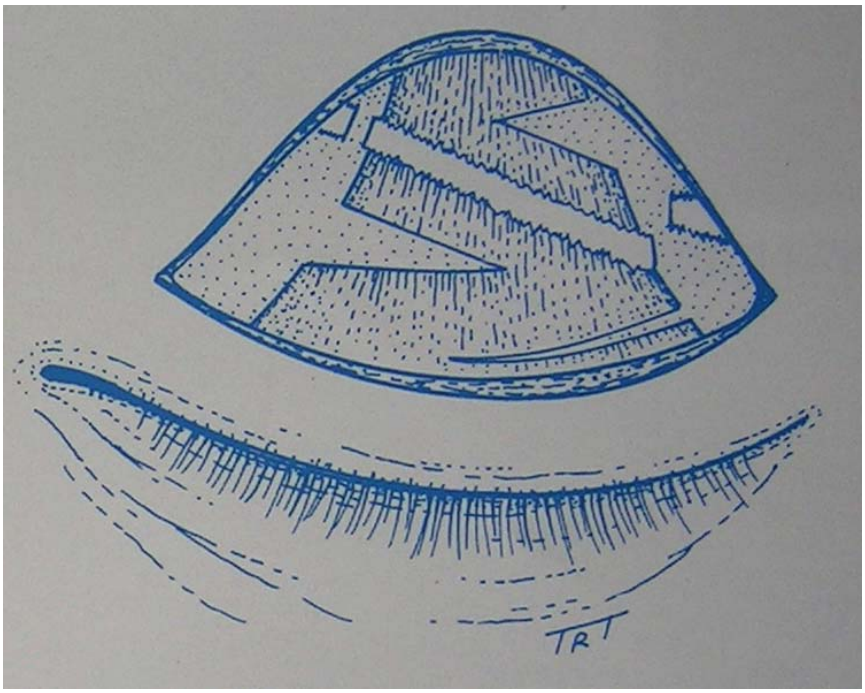
- ‘Z’ MYOTOMY in 5 patients

In our special clinic patients, especially young females complained of cosmetic problems due to lid retraction and they did not have visual impairment. These patients were selected for ‘Z’ myotomy after their thyroid disease has been non-progressive for atleast 6 months.

After the satisfaction of selection criteria, 5 of my patients underwent ‘z’ myotomy for lid retraction with excellent results.

SCHEMATIC ILLUSTRATION OF 'Z' MYOTOMY





Z-MYOTOMY

Incision

Hooking the Levator

Dissecting, Levator aponeurosis

Levator cut in Z configuration

Post op - On the table

Post-op

SUMMARY

- Thirty cases of TRO who attended our special clinic were subjected for detailed study.
- The age group ranged from 16-60 yrs, more than 50% falling between 30-50 yrs.
- As expected in any thyroid disease, females are more affected i.e., 70%
- 63.6% showed bilateral involvement with 70% of them having axial proptosis.
- Symptoms of thyrotoxicosis were present in almost all cases.
- Bilateral lid retraction associated with even minimal proptosis is the most frequently occurring problem, for which patient needed a good cosmetic relief
- In my study no abnormality was noted because of Thryoid Related Orbitopathy in Visual Acuity, Tonometry, Pupillary reaction, Ophthalmoscopy, Fields, Colour Vision and Ocular Movements.
- More than 55% of pt. had only mild proptosis and 93% of TRO had associated thyroid swelling also.

- In doing Thyroid Function Test, 73% showed hyperthyroid, 20% hypothyroid 7% showed Euthyroid states. Radio active iodine uptake done in 9 pts, 7 of them showing hot nodules, 2 of them warm nodules. No patient had cold nodules.

- USG {B Scan} was done as a screening procedure in all cases of TRO Of these 83% showed Extra OcularMuscle enlargement in CT scan too.

- Regarding the treatement 20 patients were put on antithyroid drugs while 6 on thyroxine and 2 patients under went thyroidectomy.

- Regarding surgical modalties, most of them wanted good cosmesis and relief from starring look due to lid retraction associated with exophthalmous.

- Surgical procedure of marginal Z myotomy was carried out in 5 patients who had stable TRO and thyroid status and all of them showed great improvement, after surgery cosmetically. However, longtime followup is awaited in these patients.

CONCLUSION

- Most of the patients who come for ophthalmic department with TRO are females belonging to 30 – 50 yrs of age.

- Surprisingly they do not have visual problems (nor) show signs of optic nerve compression.

- Though many of them had toxic thyroid symptoms and swelling, even enlargement of EOM on USG, ‘B’ scan orbit and CT scan the proptosis was mostly minimal.

- Many of them were on medical Treatement associated with proptosis for thyroid and required systemic steroids for arresting progression of ophthalmic disease.

- The most important reason for consulting ophthalmologists is to get a good cosmetic appearance since many of these patients have marked lid retraction, with even minimal proptosis, cause an ugly starring look either unilaterally or bilaterally.

- Simple procedure of marginal ‘z’ myotomy gives good acceptable cosmetic results in these patients and this procedure can be done easily by all ophthalmologists and there is no requirement for special instruments and sutures. However, long term effect and results of this procedure are to be evaluated.

Part - III

PROFORMA

STUDY OF THYROID RELATED ORBITOPATHY

Name : Age & Sex : Date :

Address : Height & Weight IP/OP :

Occupation Unit

COMPLAINTS AND DURATION

a. Protrusion of eyeball
b. Watering
c. Sandy sensation/Retro bulbar discomfort.

H/O PRESENT ILLNESS

Protrusion of Eyeball / Onset

Sudden/Gradual and Progressive / Intermittant

Defective Vision

Diplopia / Colour vision / field of vision

Periocular Pain

Stationary / Progressive / Intermittent

Toxic symptoms :

Weight Loss/Tachycardia/Tremor/Sweating/Changes in the nail, skin, and hair,

H/O Heat Intolerance/Cold Intolerance : Tuberculosis/Diabetes Mellitus / Hypertension

PAST HISTORY

Thyroid Dysfunction / Malignancy / Trauma / Sinus.

PERSONAL HISTORY :

MENSTRUAL HISTORY :

FAMILY HISTORY :

PHOTOGRAPH :

COMPARISON

LOCAL EXAMINATION :

LIDS	**HI**	**H**
Dalrymple Sign (Lid Retrction)		
Von Graefe sign (Upperlid-lag on downgaze)		
Kocher sign (Starring and frightened appearance)		
Stellwag sign (Infrequent blinking)		
Rosenbach sign (Tremor of the closed lid)		
Grove sign (Upper lid resistance to downward traction)		
Griffith sign (Lower-lid lags behind the globe on upward gaze)		
Means sign (Globe lags behind upper lid on upgaze)		
Jellinek sign (Increased pigmentation of the lidskin)		
Gifford sign (Prevent eversion of upper lid)		
Enroth sign (Fullness of the eyelids)		
Mobius sign (Weakness of Convergence)		

CONJUNCTIVA :

Chemosis / Hyperaemia / superior limbic Keratoconjunctivitis

CORNEA :

Exposure Keratitis / Ulcer / Keratoconjunctivitis Sicca

PUPIL :

Restricted / Diplopia

DISTANT VISION	RF	LE
Without Glass		
With Glass		
NEAR VISION	RE	LE
Without Glass		
With Glass		

COLOUR VISION :

Normal / Impairment

FIELD OF VISION :

Central scotoma / Paracentral scotoma / combined

FUNDUS :

Normal / Vascular Congestion / Swelling / Atrophy of the optic nerve /

INTRAOCULAR PRESSURE :

Primary position / Differential gaze

SLIT LAMP EXAMINATION :

Presence of tortuous vessels / Hypertrophy Lateral rectus / Superior limbic Kcratoconjunctivitis

EXAMINATION OF ORBIT	RE	LE
Proptosis-Axial / Eccentric With Bruit Without Bruit		
Valsalva Compressibility / Retropulsion		
Transillumination Orbital Mass Tenderness Swelling		

EXOPHTHALMOMETRY :

BASAL : 1 Visit II Visit III Visit

FORCED DUCTION TEST :

DIPLOPIA AMOUNT : ASSESMENT

Hess Screen

EXAMINTION OF THE THYROID GLAND

Thyroid swelling : diffuse / Nodular / Multinodular

GENERAL EXAMINATION :

Pulse rate / Rhythm / Volume / Sleeping pulserate / Temperature / BP

SKIN, HAIR AND NAIL CHANGES, PRETIBIAL MYXOEDEMA

INTERDISCIPLINARY CONSULTATIONS

ENDOCRINOLOGY OB/GYN OTHERS

MEDICAL / SURGICAL ENT

INVESTIGATION :

Blood : Urine : Albumin Sugar

Thyroid Function Test

Serum

T3

T4

TSH

ULTRASONOGRAM :

Enlargement EOM / RB Fat volume / Optic Nerve

CT SCAN :

Enlargement of Extraocular muscles / Optic Nerve Compression

MRI :

FNAC / BIOPSY :

FINAL DIAGNOSIS

TREATMENT :

PREVIOUS :

Anti-thyroid drugs – Propyl-thiouracil and β-blockers/eltroxin

Radioactive iodine therapy – Corticosteroids / Cytotoxic agents / Injection botulinum toxin / Surgery.

PRESENT :

Topical therapy – Lubricant Drops

Systemic therapy – Corticosteroids / Cytotoxic agents / Anti-thyroid drugs Radiotherapy

SURGICAL THERAPY	**RE**	**LE**
Lateral tarsorrhaphy / Z. Myotomy		
Recession of Levator and Muller's Muscle Surgery		
Blepharoplasty		
Orbital Decompression		
One wall / Two wall / Three wall & Four Wall		

FOLLOW-UP ADVICE :

INDEX TO THE MASTER CHART

1. Serial number
2. Name
3. Age
4. Sex
5. Weight
6. Complaints & Duration
    a. Protrusion of eyeball
    b. Watering of eye
    c. Sandy sensation / Retrobulbar discomfort
7. Protrusion of Eyeball
    S. Sudden
    G. Gradual
    P. Progressive
    I. Intermitent
8. Toxic Symptoms
    * Weight Loss
    O Tachycardia
    ▼ Tremor
    ❑ Sweating
    ♦ Changes in nail / skin / hair
9. Lid Signs
    1. Dalrymple sign
    2. Von Graefe sign
    3. Kocher sign
    4. Stellwag sign
    5. Rosenbach sign
    6. Grove sign
    7. Griffith sign
    8. Means sign
    9. Jellineck sign
    10. Gilford sign
    11. Enroth sign
    12. Mobius sign
10. Fundus
    N. Normal
    P. Papilloedema
11. IOP
12. SLE – Slit Lamp Examination
    i. Presence of tortuous vessels
    j. Hypertrophy of lateral rectus
    k. Superior limbic keratoconjuntivitis
13. Visual Activity

14. Orbital Proptosis
    - A. Axial
    - E. Eccentric
15. Exophthalmometry
16. Thyroid Examination
    - D. Diffuse
    - N. Nodular
    - MN. Multi nodular
17. Thyroid Function Test
    - ↓ Decreased
    - ↑ Increased
    - \- Normal

18. Thyroid Uptake Scan
    - α Hot Nodule
    - β Warm nodule
    - γ Cold nodule
19. USG orbit
    - MT. Muscle thickening
20. CT Scan
    - EOM – Extra ocular muscle enlargement
21. FNAC Thyroid
    - HT. Hyper thyroid picture
    - NT. Normal Thyroid picture
22. Past Treatment
    - AT. Antithyroid
    - S. Surgery
    - R. Radioactive iodine
23. Present Treatment
    - LD. Lubricating Drops
    - OS. Oral Steroids
    - OR. Orbital Irradiation
    - I. Immunosuppression
24. Surgical Treatment Eyelid / Orbit

MASTER CHART

1	2	3	4	5	6	7	8	9		10	11		12	13		14		15		16	17			18	19	20	21	22	23	24
								RE	LE		RE	LE		RE	LE	RE	LE	RE	LE		T3	T4	TSH							
1	Dowlath	37	F	60	a c	G	-	1,2	-	N	17.3	17.3	-	6/9	6/9	A	A	21	22	D	↑	↑	↓	β	MT	EOM	-	AT	LD/OS	
2	Shankar	27	M	56	a b	G	-	1,2,3,6	3	N	14.6	14.6	I	6/6	6/6	A	A	21	22	D	↑	↑	↓	α	MT	EOM	-	AT	LD/RT	
3	Malar	35	F	40	a c	P	* o ▼ ❑	1,2	-	N	17.3	14.6	-	6/6	6/6	A	A	21	23	N	↑	↑	↓	α	N	-	-	AT	LD/OS	Z Myotomy
4	Pitchaiammal	60	F	48	c	G	* - ▼ ❑	1,2	-	N	10.2	14.3	-	6/24	6/60	A	A	21	22	N	↑	↑	↓	–	N	-	-	AT	LD	
5	Lakshmi	42	F	47	b	-	* - ▼ -	2	-	N	17.3	17.3	-	6/6	6/6					D	↑	↑	↓	–	N	-	-	AT	LD/OS	
6	Ranjankani	16	F	26	a c	P	* - - ❑	1,2,3	1,2,3,5,6	N	17.3	17.3	-	6/6	6/6	A	A	22	24	MN	↑	↑	↓	α	MT	EOM	-	AT	LD/OS	Z Myotomy
7	Ramasamy	50	M	48	a c	G	- o ▼ -	1,2	1,2	N	14.6	14.6	-	5/60	5/60	A	A	21	22	MN	↑	↑	↓	α	MT	EOM	-	AT	LD/OS	
8	Veeraraghavan	27	M	46	a c	G	o ▼ ❑	1,2,3,4,8,9,11	-	N	20.1	17.3	-	6/6	6/6	A	A	22	21	D	↑	↑	↓	–	N	-	-	S	LD/OS (Ims)	
9	Sumathy	27	F	46	a c	P	* - - - -	1,2,3	2,3,5,6,7	N	14.6	14.6	-	6/6	6/6	A	A	22	20	MN	↑	↑	↓	α	MT	EOM	-	AT	LD/OS	
10	Suresh	22	M	50	a c	G	* - - - -	2,4	2	N	17.3	17.3	-	6/6	6/6	A	A	22	24	N	↓	↓	↑	–	N	-	-	AT	LD/OS	
11	Shanthy	32	F	82	b	G	-	1	1	N	17.3	17.3	-	6/6	6/6	A	A	21	22	D	↓	↓	↑	–	N	-	-	Eltroxin	LD	
12	Jhansi Rani	28	F	58	b c	-	-	-	-	N	17.3	17.3	-	6/6	6/6						↑	↑	↓	–	N	-	-	Eltroxin	LD	
13	Murugan	45	M	65	a b	G	-	1,3,7,8,10,12	1,2,3	N	17.3	17.3	-	6/6	6/6	A	A	22	24	D	↑	↑	↓	–	MT	EOM	HT	AT	LD/OS	Orbital Decompression
14	Perumal	39	M	55	a c	P	* - - - -	1,3	1,3	N	17.3	17.3	-	6/6	6/6	A	A	24	22	N	↑	↑	↓	–	MT	EOM	-	AT	LD/OS	
15	Sharmila	22	F	36	a	P	* o ▼ ❑	1,5	1,5	N	17.3	17.3	-	6/6	6/6	A	A	22	21	MN	↓	↓	↑	–	N	-	-	Eltroxin	LD	
16	Dayamani	35	F	48	b	-	-	-	-	N	14.6	14.6	-	6/6	6/18					N	↑	↑	↓	–	N	-	-	S/AT	LD/OS	

17	lakshmi	31	F	60	b	-	-	-	-	N	14.6	14.6	-	6/6	6/6						↓	↓	↑	–	N	-	NT	Eltroxin	LS	
18	Shalma	38	F	56	b	P	- - ▼ -	4	1,2,3	N	17.3	17.3	-	6/6	6/6	A	A	24	21	D	↓	↓	↑	–	MT	-	-	Eltroxin	LS	Z Myotomy
19	Rajeswari	37	F	60	b	G	- - ▼ -	2,9	2,3,5,9	N	17.3	17.3	-	6/12	6/6	A	A	24	21	D	↑	↑	↓	–	N	-	-	AT	LD/OS	
20	Vijayalakshmi	25	F	45	b	-	-	2,3	2,3	N	17.3	17.3	-	6/6	6/6					D	↑	↑	↓	–	N	-	-	AT	LD/OS	
21	Vasuki	35	F	60	b	-	-	1	1,2	N	17.3	17.3	-	6/6	6/6	A	E	21	22	D	N	N	↓	–	N	-	-		LS	
22	Vijaya	35	F	60	a b	G	* o ▼ ❑	1,3,4	1,3,4,8	N	17.3	17.3	-	6/60	6/60					N	N	N	↓	–	N	-	-		LS	
23	Zareena	33	F	46	a b c	G	- - ▼ ❑	1,2,3,4,6	1,2,4,5,6	N	14.6	14.6	-	6/6	6/6	A	A	24	22	D	↑	↑	↓	–	N	-	HT	AT	LD/OS	
24	Fathima	17	F	35	a	G	* - - ❑	5	1,5	N	17.3	12.2	-	6/9	6/9	A	A	21	23	D	↑	↑	↓	β	MT	EOM	-	AT	LD/OS	
25	Nirmala	35	F	60	a c	P	- - - - ♦	-	1	N	14.6	14.6	-	6/6	6/6	A	A	21	23	D	↑	↑	↓	–	N	-	-	AT	LD/OS	
26	Dhanalakshmi	38	F	55	c	G	-	1,2,3,4,6	1,5	N	17.3	17.3	-	6/6	6/6					D	↑	↑	↓	–	MT	Absent	-	AT	LD/OS	Z Myotomy
27	Mohanavel	39	M	58	a c	G	* - ▼ -	1	1	N	14.6	14.6	-	6/6	6/6	A	A	21	21	D	↑	↑	↓	α	N	-	-	AT	LD/OS	Z Myotomy
28	Justin Paul	30	M	62	a b	G	-	2	2	N	17.3	17.3	-	6/6	6/6	A	A	21	22	D	↑	↑	↓	–	MT	EOM	-		LD/OS	
29	Abaraj	60	M	60	a c	G	* - - - -	1,3	1,3	N	14.6	17.3	-	6/24	6/24	A	A	21	22	D	↑	↑	↓	α	N	-	-	AT	LD/OS	
30	Subhashini	27	F	50	b	-	-	-	-	N	17.3	17.3	-	6/9	6/9					D	↓	↓	↑	–	N	-	-	Eltroxin	LS	

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